Restorative treatments of dystrophin expression in Duchenne muscular dystrophy: A systematic review

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To evaluate the effect of pharmacological treatments that increase the synthesis of dystrophin in Duchenne muscular dystrophy (DMD). Systematic searches were carried out in MEDLINE, EMBASE, and Web of Science, and in gray literature from inception to December 2019. Clinical trials addressing the effect of restorative treatments of dystrophin expression in children and adolescents with DMD on functional outcomes {(6-minute walking distance [6MWD], other timed functional tests [TFTs], The North Star Ambulatory Assessment)}, dystrophin expression, cardiorespiratory function, and biochemical tests were included. The DerSimonian-Laird method was used to calculate the pooled estimates for functional outcomes. Eleven studies were included in the systematic review and five in the meta-analysis. Eteplirsen showed a significant effect on 6MWD, ?6MWD = 67.3 m (95% CI: 27.32, 107.28), and ?6MWD = 151.0 m (95% CI: 36.15, 265.85) at 48 weeks and 3 years, respectively. In the systematic review, analyzing individually the clinical trials using Ataluren and Drisapersen showed a nonsignificant effect on 6MWD. However, the meta-analysis showed a significant effect on 6MWD for Ataluren and Drisapersen, ?6MWD = 18.3 m (95% CI: 1.0, 35.5) and ?6MWD = 21.5 m (95% CI: 4.7, 38.3), respectively. There were no significant differences according to baseline age for Drisapersen. Similarly, the meta-analysis showed effect in TFT with Ataluren. All drugs induced a partial synthesis of dystrophin, and exon skipping was obtained with Eteplirsen and Drisapersen. Eteplirsen also improved forced vital capacity (?%pFVC = 1.8%) and maximal inspiratory pressure (?%pMIP = 4.4%). Eteplirsen and

Ataluren could modestly reduce disease progression. However, more trials are needed to confirm its efficacy, as well as quality of life and cost-utility studies.